AUG 2 3 2000

NDA 20-204/S-010

Bayer Consumer Care Division
Attention: Karen Mancuso
36 Columbia Road
P.O. Box 1910
Morristown, NJ 07962-1910

Dear Ms. Mancuso:

Please refer to your supplemental new drug application dated September 13, 1999, received September 14, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Aleve Tablets, Caplets and Gelcaps (naproxen sodium), 220 mg.

This "Changes Being Effected" supplemental new drug application provides for revised labeling to implement the allergy alert statements required by our September 15, 1998 letter, and the alcohol warning required by the final rule published on October 23, 1998 (63 FR 56789).

We have completed the review of this supplemental new drug application and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the final printed labeling submitted on September 13, 1999. Accordingly, the supplemental new drug application is approved effective on the date of this letter.

We request that the following revisions in the labeling for this drug product be implemented within 180 days or at the next printing, whichever comes first:

1. In the Allergy Alert statement, the letter "A" in "alert" should be in lower case.

2. Under "Stop use and ask a doctor if," the first bulleted statement should appear as two sentences and should read: "an allergic reaction occurs. Seek medical help right away."

3. In the Alcohol warning, the “W” in “warning” should be in lower case.

4. The first bulleted statement under each subheading, **“Do not use”** and “**Stop use and ask a doctor if**" should be included on the immediate container label.

5. The storage information should be revised to read, “store at 20- 25°C (68 - 77°F)” and “avoid humidity and excess heat 40°C (104°F).”

Furthermore, we note that the labeling was not submitted in Drug Facts format consistent with the requirements of the March 17, 1999 FEDERAL REGISTER document “Over-the-Counter Human Drugs; Labeling Requirements; Final Rule” (64 FR 13254) (OTC labeling final rule), which has been incorporated into the regulations at 21 CFR 201.66. We remind you that the labeling of your product must be revised to reflect the Drug Facts format within the timeframes specified in the OTC labeling final rule.

If a letter communicating important information about this drug product (i.e., a “Dear Health Care Practitioner” letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MED WATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857.

We remind you that you must comply with the requirements for an approved NDA set forth under2l CFR3l4.80 and 314.81.

If you have any questions regarding this application, please contact Thomas Parmelee, Pharm.D., Regulatory Project Manager, at 301-827-2271.

Sincerely

Linda M. Katz, M.D., M.P.H.
Deputy Director
Division of Over-the-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

ALEVE® Caplets

Active Ingredients

Active Ingredient (in each caplet*) Naproxen sodium 220 mg (naproxen 200 mg)

Purpose

Pain reliever / fever reducer

*capsule-shaped tablet

Uses

Temporarily relieves minor aches and pains due to:
· common cold
· headache
· toothache
· muscular aches
· backache
· menstrual cramps
· minor pain of arthritis
· temporarily reduces fever

Warnings

Allergy Alert:
Naproxen sodium may cause a severe allergic reaction which may include:
· hives
· facial swelling
· asthma (wheezing)
· shock

Alcohol Warning:
If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take naproxen sodium or other pain relievers/fever reducers. Naproxen sodium may cause stomach bleeding.

Do not use:
· with any other pain reliever
· for more than 10 days for pain
· for more than 3 days for fever
· if you have ever had an allergic reaction to any other pain reliever

Ask a doctor before use if you have ever had serious side effects from any pain reliever**.**

Ask a doctor or pharmacist before use if you are:
· taking other drugs on a regular basis
· under a doctor's care for any continuing condition

Stop use and ask a doctor if:
· an allergic reaction occurs. Seek medical help right away.
· the painful area is red and swollen
· any new or unexpected symptoms occur
· symptoms continue or worsen
· you have difficulty swallowing
· it feels like the pill is stuck in your throat

· you develop heartburn
· stomach pain occurs with use of this product or if even mild symptoms persist

If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use naproxen sodium during the last three months of pregnancy unless specifically directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.

Keep out of reach of children.

In case of accidental overdose, seek professional assistance or contact a Poison Control Center immediately.

Directions

· Drink a full glass of water with each dose.
· Do not take more than 2 caplets* in any 8 - 12 hour period
· Do not take more than 3 caplets* in a 24 hour period.

Over age 65: Do not take more than 1 caplet* every 12 hours unless directed by a doctor.

12 - 65 years: 1 caplet* every 8 - 12 hours. For the first dose you may take 2 caplets* within the first hour. The smallest effective dose should be used.

Under 12 years: Do not give this product to children under 12 unless directed by a doctor.

*capsule-shaped tablet

Other information

· Each caplet* contains: sodium 20mg
· Store at room temperature: Avoid high humidity and excessive heat 104°F (40°C)
*Capsule-shaped tablet(s)

Inactive Ingredients

magnesium stearate, microcrystalline cellulose, opadry YS-1-4215, povidone, talc

Questions or Comments?

1-800-395-0689

ALEVE® Tablets

Active Ingredients

Active Ingredient (in each tablet) Naproxen sodium 220 mg (naproxen 200 mg)

Purpose

Pain reliever / fever reducer

Uses

Temporarily relieves minor aches and pains due to:
· common cold
· headache
· toothache
· muscular aches
· backache
· menstrual cramps
· minor pain of arthritis
· temporarily reduces fever

Warnings

Allergy Alert:
Naproxen sodium may cause a severe allergic reaction which may include:
· hives
· facial swelling
· asthma (wheezing)
· shock

Alcohol Warning:
If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take naproxen sodium or other pain relievers/fever reducers. Naproxen sodium may cause stomach bleeding.

Do not use:
· with any other pain reliever
· for more than 10 days for pain
· for more than 3 days for fever
· if you have ever had an allergic reaction to any other pain reliever

Ask a doctor before use if you have ever had serious side effects from any pain reliever**.**

Ask a doctor or pharmacist before use if you are:
· taking other drugs on a regular basis
· under a doctor's care for any continuing condition

Stop use and ask a doctor if:
· an allergic reaction occurs. Seek medical help right away.
· the painful area is red and swollen
· any new or unexpected symptoms occur
· symptoms continue or worsen
· you have difficulty swallowing
· it feels like the pill is stuck in your throat
· you develop heartburn

· stomach pain occurs with use of this product or if even mild symptoms persist

If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use naproxen sodium during the last three months of pregnancy unless specifically directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.

Keep out of reach of children.

In case of accidental overdose, seek professional assistance or contact a Poison Control Center immediately.

Directions

· Drink a full glass of water with each dose.
· Do not take more than 2 tablets in any 8 - 12 hour period
· Do not take more than 3 tablets in a 24 hour period.

Over age 65: Do not take more than 1 tablet every 12 hours unless directed by a doctor.

12 - 65 years: 1 tablet every 8 - 12 hours. For the first dose you may take 2 tablet within the first hour. The smallest effective dose should be used.

Under 12 years: Do not give this product to children under 12 unless directed by a doctor.

Other information

· Each tablet contains: sodium 20mg
· Store at room temperature: Avoid high humidity and excessive heat 104°F (40°C)

Inactive Ingredients

magnesium stearate, microcrystalline cellulose, opadry YS-1-4215, povidone, talc

Questions or Comments?

1-800-395-0689

ALEVE® Gelcaps

Active Ingredients

Active Ingredient (in each gelcap*) Naproxen sodium 220 mg (naproxen 200 mg)

Purpose

Pain reliever / fever reducer

*gelatin coated capsule-shaped tablet

Uses

Temporarily relieves minor aches and pains due to:
· common cold
· headache
· toothache
· muscular aches
· backache
· menstrual cramps
· minor pain of arthritis
· temporarily reduces fever

Warnings

Allergy Alert:
Naproxen sodium may cause a severe allergic reaction which may include:
· hives
· facial swelling
· asthma (wheezing)
· shock

Alcohol Warning:
If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take naproxen sodium or other pain relievers/fever reducers. Naproxen sodium may cause stomach bleeding.

Do not use:
· with any other pain reliever
· for more than 10 days for pain
· for more than 3 days for fever
· if you have ever had an allergic reaction to any other pain reliever

Ask a doctor before use if you have ever had serious side effects from any pain reliever**.**

Ask a doctor or pharmacist before use if you are:
· taking other drugs on a regular basis
· under a doctor's care for any continuing condition

Stop use and ask a doctor if:
· an allergic reaction occurs. Seek medical help right away.
· the painful area is red and swollen
· any new or unexpected symptoms occur
· symptoms continue or worsen
· you have difficulty swallowing

· it feels like the pill is stuck in your throat
· you develop heartburn
· stomach pain occurs with use of this product or if even mild symptoms persist

If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use naproxen sodium during the last three months of pregnancy unless specifically directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.

Keep out of reach of children.

In case of accidental overdose, seek professional assistance or contact a Poison Control Center immediately.

Directions

· Drink a full glass of water with each dose.
· Do not take more than 2 gelcaps* in any 8 - 12 hour period
· Do not take more than 3 gelcaps* in a 24 hour period.

Over age 65: Do not take more than 1 gelcap* every 12 hours unless directed by a doctor.

12 - 65 years: 1 gelcap* every 8 - 12 hours. For the first dose you may take 2 gelcaps* within the first hour. The smallest effective dose should be used.

Under 12 years: Do not give this product to children under 12 unless directed by a doctor.

*gelatin coated capsule-shaped tablet

Other information

· Each gelcap* contains: sodium 20mg
· Store at room temperature: Avoid high humidity and excessive heat 104°F (40°C)
*gelatin coated Capsule-shaped tablet(s)

Inactive Ingredients

D&C Yellow #10 Lake, edetate disodium, edible ink, FD&C Blue #1, FD&C Yellow #6 Lake, gelatin, glycerin, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, povidone, stearic acid, talc, titanium dioxide, and triacetin.

Questions or Comments?

1-800-395-0689